

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

Claims 1 - 3 (*cancelled*)

4. (*currently amended*) A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, comprising 1-5 targeting moieties.

5. (*currently amended*) A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, comprising one targeting moiety.

Claims 6 - 11 (*cancelled*)

12. (*currently amended*) A ~~compound~~ **radiopharmaceutical** according to claim ~~1~~ **47**, wherein **the linking group is of the formula:**



W¹ is C(=O)NR¹⁵;

h is 1;

g is 3;

R¹³ and R¹⁴ are independently H;

x is 1;

k is 0;

g' is 0;

h' is 1;

W² is NH; and

x' is 1.

13. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47,

wherein the linking group is of the formula:



x is 0;

k is 1;

Z is aryl substituted with 0-3 R¹⁶;

g' is 1;

W² is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

14. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47,

wherein the linking group is of the formula:



W¹ is C(=O)NR¹⁵;

h is 1;

g is 2;

R¹³ and R¹⁴ are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C₁₋₅ alkyl substituted with 0-3 R¹⁶;

R¹⁶ is SO₃H;

W² is NHC(=O) or NH;

h' is 1; and

x' is 2.

15. *(cancelled)*

16. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47,
wherein:

x is 0;
k is 0;
g' is 3;
h' is 1;
W² is NH; and
x' is 1.

17. *(cancelled)*

18. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47,
wherein the linking group is of the formula:



W¹ is C=O;
h is 0, 1, or 2;
g is 2;
R¹³ and R¹⁴ are **independently** H;
x is 0, 1, 2, 3, 4, or 5;
k is 0;
g' is 0;
h' is 1;
W² is NH; and
x' is 1.

19. *(currently amended)* A ~~compound~~ radiopharmaceutical according to claim ~~10~~ 47,
wherein the linking group is absent.

Claims 20 - 46 (*cancelled*)

47. (*currently amended*) A radiopharmaceutical comprising a compound ~~of claim 1~~ and a cytotoxic radioisotope which is complexed to the chelator;

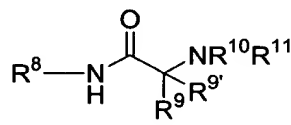
wherein said compound comprises:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <100 nM of the formulae (Ia) or (Ib):



wherein,

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group, provided that when R^8 is phenyl, R^{10} is $-\text{C}(=\text{O})-\text{CHR}^{12}-\text{NH}-\text{CH}(\text{CH}_3)-\text{COOH}$;

R^9 and $\text{R}^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group, or are taken together with the carbon atom to which R^9 and $\text{R}^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted a bond to the linking;

or alternatively,

R⁹ and R¹⁰ are taken together with the nitrogen atom and carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 additional heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with a bond to the linking group; and

R¹² is independently C₁₋₂₀ alkyl.

Claims 48 - 49 (*cancelled*)

50. (*currently amended*) A radiopharmaceutical ~~according to claim 49~~

~~wherein the compound is~~ selected from the group consisting of:

2-{{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

2-{{[5-(4-{{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

wherein the cytotoxic radioisotope is ^{99m}Tc.

51. (*original*) A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of beta particle emitters, alpha particle emitters, and Auger electron emitters.

52. (*original*) A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁴⁹Pm, ⁹⁰Y, ²¹²Bi, ¹⁰³Pd, ¹⁰⁹Pd, ¹⁵⁹Gd, ¹⁴⁰La, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁶⁵Dy, ¹⁶⁶Dy, ⁶⁷Cu, ¹⁰⁵Rh, ¹¹¹Ag, and ¹⁹²Ir.

53. *(original)* A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , and ^{105}Rh .

54. *(original)* A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , and ^{212}Bi .

55. *(cancelled)*

56. *(previously amended)* A radiopharmaceutical composition comprising a radiopharmaceutical of claim 47, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

Claims 57 - 60 *(cancelled)*

61. *(previously amended)* A radiopharmaceutical kit comprising a radiopharmaceutical of claim 47, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

62. *(currently amended)* A kit of ~~Claim 60~~ claim 61 further comprising a stabilizer.

63. *(original)* A radiopharmaceutical kit according to claim 61, wherein the radioisotope is ^{186}Re or ^{188}Re and the kit further comprises one or more ancillary ligands and a reducing agent.

64. *(original)* A radiopharmaceutical kit according to claim 63, wherein the ancillary ligands are tricine and a phosphine.

Claims 65 - 67 (*cancelled*)

68. (*previously amended*) A method of treating a pathological disorder mediated by a matrix metalloproteinase in a patient which comprises ~~administering~~ administering to a patient in need thereof a therapeutically effective amount of a radiopharmaceutical according to claim 47 and a pharmaceutically acceptable carrier.

Claims 69 - 71 (*cancelled*)

72. (*original*) A method of inhibiting proliferation of cancer cells, comprising contacting the cancer cells with a proliferation-inhibitory amount of a radiopharmaceutical of claim 47.

73. (*previously amended*) A method of claim 68, wherein the matrix metalloproteinase is selected from the group consisting of: MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

74. (*previously amended*) A method of claim 68 wherein the matrix metalloproteinase is selected from the group consisting of: MMP-2, MMP-9, and MMP-14.

Claims 75 - 77 (*cancelled*)

78. (*currently amended*) A process for the preparation of a radiopharmaceutical, said process comprising generating a macrostructure from a plurality of molecular components wherein the plurality of components ~~includes a compound of claim 1 and a cytotoxic radioisotope~~ comprises a radiopharmaceutical according to claim 47.

79. (*cancelled*)